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Exclusion of Progressive Brain Disorders of Childhood for a Cerebral Palsy Monitoring System: A Public Health Perspective

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Abstract

Background—Cerebral palsy (CP) is defined by its nonprogressive features. Therefore, a standard definition and list of progressive disorders to exclude would be useful for CP monitoring and epidemiologic studies.

Methods—We reviewed the literature on this topic to 1) develop selection criteria for progressive brain disorders of childhood for public health surveillance purposes, 2) identify categories of disorders likely to include individual conditions that are progressive, and 3) ascertain information about the relative frequency and natural history of candidate disorders.

Results—Based on 19 criteria that we developed, we ascertained a total of 104 progressive brain disorders of childhood, almost all of which were Mendelian disorders.

Discussion—Our list is meant for CP surveillance programs and does not represent a complete catalog of progressive genetic conditions, nor is the list meant to comprehensively characterize disorders that might be mistaken for cerebral palsy. The criteria for progressive disorders that we developed could be applied by public health investigators in the future, as more children with very rare conditions are followed and new candidate disorders are identified.

Keywords

cerebral palsy; neurodegenerative disease; population surveillance; public health

Introduction

Cerebral palsy (CP) is defined as “a group of permanent disorders of the development of movement and posture, causing activity limitation, that are attributed to nonprogressive disturbances that occurred in the developing fetal or infant brain.”[1] Historically, the idea of nonprogression has always been a part of the definition of CP. Minear,[2] who polled the membership of the American Academy of Cerebral Palsy in 1953, found that certain conditions were generally excluded: transient conditions, neoplasms, progressive disorders, and spinal cord disorders. Interestingly, these are still agreed-upon CP excludable conditions. Clinicians and researchers alike would seem to agree that “motor dysfunction

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which results from recognized progressive brain disorders is not considered CP."[3] While examples of such disorders have been published, drawn from cases found by population-based surveillance programs in Europe and Australia,[4,5] we have not found a standard list of conditions that are considered progressive in registry management based on a literature review.

CP is a clinical condition, defined by history and physical findings, therefore diagnostic assessments are generally guided by clinical indications or suspicion of identifiable abnormalities.[6] In 2004, the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society published a practice parameter that included an algorithm to assist with the diagnostic assessment of children with suspected CP.[7] Whereas laboratory testing is not necessary to identify CP or its subtypes, studies of children with CP reviewed in the practice parameter found that a majority will have abnormalities on computed tomography (average, 77%, range, 62%–93%) or magnetic resonance imaging (average, 89%; range, 68%–100%). Metabolic or genetic testing has yielded abnormal results in children with CP less frequently, but such testing has been a consideration if the child has atypical features such as evidence of deterioration.[7] Particularly for nonspastic clinical presentations associated with ataxia, dyskinesia, or hypotonia, confidence in CP categorization occurs only after assessments have been done for other possible neurological disorders (many of which are progressive). Therefore, surveillance personnel abstracting medical records and physicians caring for children with CP must be aware of specific neurological, genetic, and metabolic conditions that they might encounter.

The genesis of this literature review was a desire to construct a list of progressive conditions that most would agree are not CP, to assist nonphysician field staff reviewing and abstracting medical and education records in a community setting as part of the Autism and Developmental Disabilities Monitoring Network. This Network is a multisite, collaborative program funded by the Centers for Disease Control and Prevention to monitor the occurrence of developmental disabilities, including CP, in 8-year-old children across the United States.[8] In this exploratory effort, our goal was to identify a list of brain disorders of childhood that by nature of their underlying pathophysiology and prognosis would not meet the nonprogressive component of the definition for CP. In this report, we present the methods for creating our list of progressive brain disorders of childhood and the table of such conditions identified to date.

Methods

Criteria for Progressive Brain Disorders of Childhood

As our first goal, we developed criteria for progressive disorders to apply in our literature review (Table 1). Since this activity was focused on a case definition for public health surveillance of CP, in particular for the Autism and Developmental Disabilities Monitoring Network, we concentrated on disorders with progressive features typically occurring by 8 years of age.[8] By definition, we did not consider conditions that are purely myopathies, disorders only involving the spinal cord, or peripheral neuropathies (neuromuscular disorders), since the primary pathology in these conditions is not in the brain. Progressive

features were defined primarily by loss of motor skills or milestones, although descriptions of disorders often more broadly described generalized regression, deteriorating clinical courses or neuropathological findings, or normal early development with subsequent developmental delay. If a disorder was clearly a neurodegenerative condition, we decided to list it for the purposes of exclusion from surveillance, even if some of the neurologic findings progressed and others did not. Another important feature that we considered was childhood mortality; lethality alone was not a criterion for progressiveness, since some genetic conditions known for mortality due to malformations or pathophysiologic processes outside of the central nervous system can have static or even improving neurologic manifestations.

The criteria took into account what is typical or described in the majority of children with disorders in question. The rationale for this principle was our belief that when neurologic deterioration is a rare feature, typical children with certain diagnoses who might have CP-like features for reasons unrelated to the disorder should not be excluded categorically. In practice, a limitation of applying this principle was the inadequate precision of literature quantifying the occurrence of CP-like features in rare genetic conditions. The issue of the effects of available therapies on natural history also is problematic, including the spectrum of interventions from diet and medications to enzyme replacement and stem-cell transplantation. Unfortunately, with our routine surveillance procedures, without a special study it is typically difficult to ascertain variables such as treatment regimens and timing of therapies that might be important in assessing the adequacy of treatment and its relationship to the clinical outcome of a particular child.[9] For our list of progressive disorders, we did not review the core disorders on the Recommended Uniform Screening Panel for newborns in the United States,[10] since the typical outcome for these conditions has changed because treatment is routinely instituted shortly after birth, thus preventing progressive features, eg, hypotonia and intellectual disability with congenital hypothyroidism. For other conditions with more potential variability in treatment in the general population, we did not consider the effects of such therapies on natural histories, eg, hematopoietic stemcell transplantation in Krabbe disease. The rapid progress expected in the diagnosis and treatment of progressive disorders, with concomitant changes in newborn screening panels as well as clinical practice, is another caveat for the need to continuously update surveillance practices.

Selection Process for Categories of Candidate Conditions

After developing criteria for our literature review, the next step was to identify broad categories of disorders that were likely to include individual conditions that are progressive, such as leukodystrophies and lysosomal storage diseases. Ideas for these categories sometimes were generated by a particular disorder found in CP review articles or chapters,[4,5,11–13] but we also attempted to identify potential categories through a search for progressive or degenerative disorders in published literature. Due to a lack of epidemiologic literature, we did not perform a formal meta-analysis but used standardized methods to review primarily expert literature (standard genetics textbooks, review articles, and selected online resources used in clinical practices and medical school courses). After a category of disorders was identified, we created a list of individual conditions within the category to

review using overview chapters, indices, and summary tables in such literature.[14–27] Occasionally, a new class was added after a query about a particular case by field staff.

Reviews of Candidate Conditions

Next, we searched for information about the natural history of candidate disorders in textbooks, review articles, and online catalogs[14–27]; if necessary, we evaluated primary sources of natural history data referenced therein or searched databases such as PubMed. Not uncommonly, natural history descriptions and neurologic manifestations were not mentioned in a particular review article or chapter, but only if 2 or more comprehensive sources lacked any information about a progressive course was the disorder left off our final list. A particularly important impetus for reviewing primary sources of information was when one source described a progressive neurologic feature but others did not. For example, the term *progressive spasticity* is used in connection with Weaver syndrome in a highly-cited textbook,[18] but in a review by Opitz, Weaver, and Reynolds, this complication was described in only 1 child who also had spinal cord compression.[28] Similarly, as noted in Table 1, we did not consider a condition to be a progressive disorder when deterioration tended to occur from repeated strokes or seizures per se, rather than events in the brain secondary to a neurodegenerative process.

Special Considerations for Conditions with High Rates of Fetal Death or Early Mortality

For surveillance purposes, we did not include conditions with high rates of fetal death or early mortality since the minimum age of CP diagnosis for inclusion in our monitoring program was 2 years (Table 1). For rare disorders, high rates of mortality are obviously problematic in assessing natural histories related to motor milestones, particularly when fetal or neonatal deaths are the typical outcomes. Occasionally children with such disorders will survive long enough to be ascertained by CP surveillance systems, and in fact children with some disorders described as lethal in older references are now treated surgically or with new medical interventions, and are gaining skills in special education settings. Our practice for such conditions is to make decisions about whether they should be excluded from CP surveillance on a case-by-case basis after they have been abstracted, rather than categorically labeling them as progressive disorders.

Special Considerations for Heterogeneous Conditions

We did not include groups of conditions with well-known clinical and genetic variability, such as mitochondrial neuromyopathies. Certain mitochondrial disorders were included if they resulted in a distinct syndromic phenotype that has a relatively well-defined natural history (eg, neuropathy, ataxia, and retinitis pigmentosa). Other mitochondrial disorders such as oxidative phosphorylation defects with specific electron transport complex pathology generally were not listed, since the nature of many of these conditions leads to heterogeneity of outcomes.

Some conditions such as Leigh syndrome are also heterogeneous but have a distinctive phenotype with progressive features generally included. There are also well-defined diagnostic criteria for such conditions with presumably less variability in community diagnoses. We therefore included such conditions on our list of progressive brain disorders.

Some rarer conditions, such as pontocerebellar hypoplasia, have multiple genetic subtypes (with varying natural histories) that might not necessarily be evident to nonphysician field staff, and therefore would be considered on a case-by-case basis as described above.

Results

Table 1 includes all of the criteria we developed to define and select progressive brain disorders of childhood. Since we designed these 19 criteria for CP surveillance purposes, we qualified the overriding definition of a progressive disorder with that distinction (criteria 1A and 1B). The table includes some examples of disorders for which the selection process and special considerations were notably applicable (eg, criteria 2B, 3A, or 5A).

We have listed 104 disorders that we found that met our selection criteria in Table 2. Almost all of those itemized are Mendelian disorders, so we have also listed the Mendelian Inheritance in Man (MIM) numbers currently assigned to the disorders.[20] The primary name usually corresponds to the main MIM title, but we have also listed other terms for clarity and for use by field staff.

Discussion

Many of these disorders that we identified for CP surveillance exclusion are quite rare, but together they represent a large number of affected children with individual metabolic and other genetic conditions that might be encountered by field staff. Our list does not represent a comprehensive catalog of progressive genetic conditions, nor does a condition's absence from our list necessarily have clinical implications for a favorable prognosis. Readers should also note that some of these disorders would not be mistaken for CP by astute providers in many clinical settings; nevertheless, diagnoses of these progressive disorders should signal exclusion from ascertainment by surveillance program staff.

We found this review and compilation of conditions challenging for a number of reasons. First, there are few articles with a particular focus on these surveillance questions as they relate to CP.[4,5] Hence, there is a need for this information but little to build upon. Secondly, the concept of a condition being slowly progressive is debated, but in the end, there is no consensus as to whether such a condition is considered progressive or not. Another challenge we found was with conditions where the clinical presentation varies considerably; eg, certain mitochondrial disorders. Without exact laboratory confirmation of type, how should conditions that fall within such a group be considered for possible exclusion as CP? If there is an atypical and typical form of the condition, we considered the clinical course of the typical form (eg, Rett syndrome). Any condition with a mean age of onset after age 8 or with "adult onset" or "late onset" in the name was not, for our purposes, considered a progressive disorder of childhood (eg, Friedreich ataxia).

Although this was a challenging undertaking, we think that it will have utility in surveillance and research as well as certain clinical settings. We will be applying the list in our own surveillance processes to determine its utility and validity, and in future work could analyze the practical use of this list to determine its value and to make updates. We also challenge others to critique our work and to expand upon it as more children with very rare disorders

are followed and new candidate disorders are identified. By sharing our experience, we welcome others to consider the usefulness of defining what is and is not a progressive disorder and thereby extend the work we have started.

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The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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Table 1

Public Health Surveillance Criteria for Progressive Brain Disorders of Childhood

1	A. For CP surveillance purposes, progressive disorders of childhood are those conditions causing progressive loss of motor skills (as opposed to those solely affecting memory and related dementia).
	B. The loss of motor skills must result from a recognized progressive brain disorder (as opposed to those solely of spinal, peripheral nerve or muscular origin).
2	A. For a condition to be considered a progressive disorder of childhood, the natural history of the condition should describe regression or a progressive or (neuro)degenerative course with onset during childhood. For CP surveillance purposes, "during childhood" is defined as ≤8 years old.
	B. If at least two references do not mention that the condition is progressive, then the condition is not progressive (eg, 18q-syndrome).
	C. If the typical age of onset for a progressive disorder is after age 8, then the condition is not considered a progressive disorder of childhood (eg, cerebral arteriopathy with subcortical infarcts and leukoencephalopathy – onset in midlife; earliest age in 20s).
	D. If fewer than 5 cases of a progressive disorder are reported in the literature, then the condition is not considered a progressive disorder of childhood for surveillance purposes. Rationale: a sufficient number of cases needs to be reported in the literature to obtain a general description of the natural history of the disorder.
3	A. If there are typical and atypical forms of a condition described in the literature, decide whether the condition is progressive based on what is true for the typical form of the disorder (eg, regression is seen in typical cases with Rett syndrome, but might not be a feature for atypical forms).
	B. If progression is a rare feature of a condition, do not consider the condition progressive (eg, craniometaphyseal dysplasia). Rationale: when the association is almost unheard of, do not exclude all potential children with CP who might coincidentally have the genetic condition.
	C. Conditions where progression during childhood is a possible but not universal feature (and progression is not a rare feature) will not be considered categorically progressive. Decisions about CP case status for individual children with these conditions should be made on a case by case basis through the review of the child's medical history, motor findings and clinical course rather than the diagnosis per se.
	D. Progressive disorders that typically result in stillbirth or early mortality (before age 2) will not be included. Rationale: to be included in the monitoring program, the minimum age for CP diagnosis is age 2 years. In the unlikely event that a child with one of these disorders survives until age 8 and comes into the surveillance program, the decision about CP case status will be made on a case-by-case basis through the review of the child's medical history, motor findings and clinical course.
4	A. For surveillance purposes, therapies to halt the progression of a condition will not be taken into account.
	B. Conditions that involve an accumulation of static cerebral lesions (eg, cerebrovascular complications of sickle cell disease) and predispose the child to repeated cerebral insults should not be considered progressive ("deterioration resulting from repeated insults is not the usual meaning of progressive"[4]).
	C. Conditions where seizures are a feature (eg, tuberous sclerosis): do not take deterioration resulting directly from repeated seizures ("insults"[4]) into account when deciding if the condition is progressive, as opposed to when the progressive effects of the underlying disorder cannot be separated from the associated seizures themselves, as in epileptic encephalopathies (eg, Dravet syndrome).
5	A. If the infantile/childhood form is progressive, then the condition is categorically progressive (eg, Krabbe disease or Alexander disease).
	B. Any condition with "adult onset" or "late onset" in the name is not considered a progressive disorder of childhood (eg, autosomal dominant late-onset leukoencephalopathy).
	C. If the condition is progressive during childhood and stabilizes during adulthood, then consider the condition progressive (eg, Sjogren-Larsson syndrome).
	D. If there are infantile and adult forms of a progressive condition, assume the child has the infantile form if the child shows neurologic signs during childhood.
6	A. Conditions described as acute are not considered progressive for surveillance purposes (eg, acute disseminated encephalomyelitis/ADEM).
	B. Conditions without clinical symptoms are not considered progressive for surveillance purposes (eg, extensive cerebral white matter abnormality without clinical symptoms).

Table 2

Progressive Brain Disorders of Childhood for Public Health Surveillance

MIM #	Disorder	Other Terms
258501	3-methylglutaconic aciduria, type III (MGCA3)	MGA, type III
202370	Adrenoleukodystrophy, autosomal neonatal form	Neonatal adrenoleukodystrophy (NALD)
300100	Adrenoleukodystrophy, X-linked (X-ALD)	Adrenoleukodystrophy (ALD)
225750[a]	Aicardi-Goutieres syndrome (AGS)	Aicardi-Goutieres syndrome 1 (AGS1)
203450	Alexander disease	
300523	Allan-Herndon-Dudley syndrome (AHDS)	MCT8 (SLC16A2)-specific thyroid hormone cell transporter
207800	Argininemia	Arginase deficiency
608643	Aromatic L-amino acid decarboxylase (AADC) deficiency	
208400	Aspartylglucosaminuria (AGU)	
208920	Ataxia, early-onset, with oculomotor apraxia and hypoalbuminemia (EAOH)	Ataxia with oculomotor apraxia I (AOA1)
208900	Ataxia-telangiectasia (AT)	
607483	Basal ganglia disease, biotin-responsive	
210000	Behr syndrome	
271900	Canavan disease	
214150[a]	Cerebro-oculo-facio-skeletal (COFS) syndrome	Cerebro-oculo-facio-skeletal syndrome 1 (COFS 1) Pena-Shokeir syndrome, type II
256730	Ceroid lipofuscinosis, neuronal, 1 (CLN1)	Neuronal ceroid lipofuscinosis, infantile (INCL) Santavuori-Haltia disease
204500	Ceroid lipofuscinosis, neuronal, 2 (CLN2)	Neuronal ceroid lipofuscinosis, late-infantile (LINCL) Jansky-Bielschowsky disease
204200	Ceroid lipofuscinosis, neuronal, 3 (CLN3)	Neuronal ceroid lipofuscinosis, juvenile (JNCL) Batten disease Spielmeyer-Vogt disease
256731	Ceroid lipofuscinosis, neuronal, 5 (CLN5)	
601780	Ceroid lipofuscinosis, neuronal, 6 (CLN6)	
610951	Ceroid lipofuscinosis, neuronal, 7 (CLN7)	
600143	Ceroid lipofuscinosis, neuronal, 8 (CLN8)	
609055	Ceroid lipofuscinosis, neuronal, 9 (CLN9)	
610127	Ceroid lipofuscinosis, neuronal, 10 (CLN10)	
216400	Cockayne syndrome, type A (CSA)	Cockayne syndrome, type I (CS type I)
133540	Cockayne syndrome, type B (CSB)	Cockayne syndrome, type II (CS type II)
278800	De Sanctis-Cacchione syndrome	
607208	Dravet syndrome	Severe myoclonic epilepsy in infancy (SMEI)
128230	Dystonia, dopa-responsive (DRD)	GTP cyclohydrolase 1-deficient dopa-responsive dystonia (GTPCH1-deficient DRD)
308350	Epileptic encephalopathy, early infantile, 1 (EIEE1)	West syndrome
602473	Ethylmalonic encephalopathy (EE)	
228000	Farber lipogranulomatosis	Farber disease

MIM #	Disorder	Other Terms
230000	Fucosidosis	
230900	Gaucher disease, type II (GD II)	
231000	Gaucher disease, type III (GD III)	
605899	Glycine encephalopathy (GCE)	Nonketotic hyperglycinemia (NKH)
232300	Glycogen storage disease II (GSD II)	Pompe disease
230600	GM1-gangliosidosis, type II	
612736	Guanidinoacetate methyltranferase (GAMT) deficiency	Creatine deficiency syndrome due to GAMT deficiency
b	Hereditary spastic paraplegia (HSP)	Familial spastic paraplegia (FSP)
607014	Hurler syndrome	Mucopolysaccharidosis type I H (MPS I H)
607015	Hurler-Scheie syndrome	Mucopolysaccharidosis type I H/S (MPS I H/S)
269920	Infantile sialic acid storage disorder (ISSD)	Infantile free sialic acid storage disease
245200	Krabbe disease	Globoid cell leukodystrophy (GLD/GCL)
236792	L-2-hydroxyglutaric aciduria (L-2-HGA)	
256000	Leigh syndrome (LS)	
300322	Lesch-Nyhan syndrome (LNS)	
603896	Leukoencephalopathy with vanishing white matter (VWM)	Childhood ataxia with central nervous system hypomyelination/vanishing white matter (CACH/ VWM)
248500	Mannosidosis, alpha B, lysosomal	Alpha-mannosidosis
248800	Marinesco-Sjogren syndrome (MSS)	
303350	MASA syndrome	Mental retardation, aphasia, spastic paraplegia, and adducted thumbs Spastic paraplegia-1 (SPG1)
604004	Megalencephalic leukoencephalopathy with subcortical cysts (MLC)	
309400	Menkes disease (MNK)	
250100	Metachromatic leukodystrophy (MLD)	Arylsulfatase A (ARSA) deficiency
277400	Methylmalonic aciduria and homocystinuria, cblC type	
277410	Methylmalonic aciduria and homocystinuria, cblD type	
203700	Mitochondrial DNA depletion syndrome 4A (Alpers type) (MTDPS4A)	Alpers syndrome Alpers-Huttenlocher syndrome
271245	Mitochondrial DNA depletion syndrome 7 (hepatocerebral type) (MTDPS7)	Infantile-onset spinocerebellar ataxia (IOSCA)
540000	Mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes (MELAS)	
252150	Molybdenum cofactor deficiency, complementation group A (MOCODA)	
252500	Mucolipidosis II Alpha/Beta (ML II Alpha/Beta)	Mucolipidosis II (ML II) I-cell disease
252600	Mucolipidosis III Alpha/Beta (ML III Alpha/Beta)	
252650	Mucolipidosis IV (ML IV)	
309900	Mucopolysaccharidosis type II (MPS II)	Hunter syndrome
252900	Mucopolysaccharidosis type IIIA (MPS IIIA)	Sanfilippo syndrome A
252920	Mucopolysaccharidosis type IIIB (MPS IIIB)	Sanfilippo syndrome B

MIM #	Disorder	Other Terms
252930	Mucopolysaccharidosis type IIIC (MPS IIIC)	Sanfilippo syndrome C
252940	Mucopolysaccharidosis type IIID (MPS IIID)	Sanfilippo syndrome D
253200	Mucopolysaccharidosis type VI (MPS VI)	Maroteaux-Lamy syndrome
253220	Mucopolysaccharidosis type VII (MPS VII)	Sly syndrome
272200	Multiple sulfatase deficiency (MSD)	Sulfatidosis, juvenile, Austin type
545000	Myoclonic epilepsy associated with ragged-red fibers (MERRF)	
250800	NADH-cytochrome b5 reductase deficiency, type II	Methemoglobinemia, type II
256550	Neuraminidase deficiency	Mucolipidosis I (ML I) Sialidosis type II
234200	Neurodegeneration with brain iron accumulation 1 (NBIA1)	Pantothenate kinase-associated neurodegeneration (PKAN)
256600	Neurodegeneration with brain iron accumulation 2A (NBIA2A)	Infantile neuroaxonal dystrophy (INAD)
610217	Neurodegeneration with brain iron accumulation 2B (NBIA2B)	Atypical neuroaxonal dystrophy (Atypical NAD)
551500	Neuropathy, ataxia and retinitis pigmentosa (NARP)	
257200	Niemann-Pick disease, type A (NPD-A)	
257220[a]	Niemann-Pick disease, type C (NPC)	
260565	PEHO syndrome	
312080	Pelizaeus-Merzbacher disease (PMD)	
264470	Peroxisomal acyl-CoA oxidase deficiency	
266150	Pyruvate carboxylase (PC) deficiency	
312170	Pyruvate decarboxylase deficiency	Pyruvate dehydrogenase (PDH) complex deficiency
266510	Refsum disease, infantile (IRD)	
312750	Rett syndrome (RTT)	
268800	Sandhoff disease	GM2-gangliosidosis, type II
607016	Scheie syndrome	Mucopolysaccharidosis type I S (MPS I S)
609241	Schindler disease, type I	
605407	Segawa syndrome, autosomal recessive	Tyrosine hydroxylase deficiency
604369	Sialuria, Finnish type	Salla disease
270200	Sjogren-Larsson syndrome (SLS)	
270550	Spastic ataxia, Charlevoix-Saguenay type (SACS)	Autosomal recessive spastic ataxia of Charlevoix-Saguenay (ARSACS)
312920	Spastic paraplegia 2, X-linked (SPG2)	Spastic paraplegia 2 (SPG2)
182600	Spastic paraplegia 3, autosomal dominant (SPG3A)	Spastic paraplegia 3A
300266	Spastic paraplegia 16, X-linked (SPG16)	
275900	Spastic paraplegia 20, autosomal recessive (SPG20)	Troyer syndrome
612319	Spastic paraplegia 35, autosomal recessive	Fatty acid hydroxylase-associated neurodegeneration (FAHN)
272100	Sudanophilic cerebral sclerosis	Schilder disease
272300	Sulfocysteinuria	Sulfite oxidase deficiency
272800	Tay-Sachs disease (TSD)	GM2-gangliosidosis, type I
190450	Triosephosphate isomerase (TPI) deficiency	

MIM #	Disorder	Other Terms
214100	Zellweger syndrome (ZS)	

[a] Multiple MIM (Mendelian Inheritance in Man) entries with same title root; all entries are progressive disorders; no entry has a commonly used eponym. Disorder is listed in this table with the MIM number for the most common MIM entry.

[b] General term for progressive disorder; no MIM title; all subtypes are progressive disorders.